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Items 21 - 31 of 31 Previous Page 2 of 2

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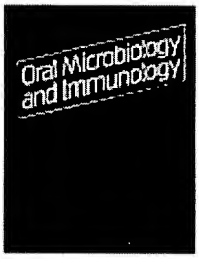

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Abstract

Induction of secretory immunity with bioadhesive poly (D,L-lactide-co-glycolide) microparticles containing *Streptococcus sobrinus* glucosyltransferase

D. J. Smith[1], D. J. Trantolo[2], W. F. King[1], E. J. Gusek[2], P. H. Fackler[2], J. D. Gresser[2], V. L. De Souza [1], D. L. Wise[2]

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Daniel J. Smith, Forsyth Dental Center, 140 The Fenway, Boston, MA 02115, USA

Abstract

The effect of mucosal delivery of *Streptococcus sobrinus* glucosyltransferase (GTF) in bioadhesive poly (D,L-lactide-co-glycolide) (PLGA) microparticles on induction of salivary IgA and serum IgG antibody responses was measured in Sprague-Dawley rats. Preparations of GTF/PLGA/gelatin microparticles, or PLGA/gelatin microparticles or GTF in alum, were administered four times at weekly intervals by intranasal or intragastric routes. Two subcutaneous injections of GTF in PLGA/gelatin microparticles or in alum were given to separate groups of rats. Significant elevations in salivary IgA antibody levels to *S. sobrinus* GTF were observed only in the groups

immunized intranasally 28 days after immunizations were begun. Five of six rats given the GTF microparticles intranasally had positive salivary IgA antibody responses to GTF, and the mean salivary IgA antibody level of this group was 30-fold higher than any other mucosally or systemically immunized group. Salivary IgA responses in the GTF-microparticle group remained significantly higher than all other mucosally immunized groups for at least 10 weeks after the primary immunization. All rats in this group demonstrated aspects of anamnesis following a more limited secondary course of intranasal administration. Intranasal administration of GTF in microparticles also induced a serum IgG response to GTF in some rats. After secondary intranasal GTF microparticle administration, several rats had sustained serum IgG antibody levels that were within the range of sera from rats subcutaneously injected with GTF in microparticles or in alum. Thus intranasal delivery of GTF-containing bioadhesive microparticles induced the highest and longest lasting salivary immune response of any mucosal or systemic route or vehicle tested and could be expected to be a useful method for induction of mucosal immunity.

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1: Tissue Eng. 2000 Jun;6(3):217-27.

Biodegradable foam coating of cortical allografts.

Bondre S, Lewandrowski KU, Hasirci V, Cattaneo MV, Gresser JD, Wise DL, Tomford WW, Trantolo DJ.

Department of Chemical Engineering, Northeastern University, Boston, Massachusetts, USA.

Clinical outcomes of bone allograft procedures may be improved by modifying the surface of the graft with an osteoconductive biopolymeric coating. In this comparative in vitro study, we evaluated the dimensional stability, mechanical strength, hydrophilicity, and water uptake of biodegradable foams of poly(propylene fumarate) (PPF) and poly(d,l-lactic-co glycolic acid) (PLGA) when applied as surface coatings to cortical bone. Cortical bone samples were divided into four groups: Type I, untreated bone; Type II, laser-perforated bone; Type III, partially demineralized bone; and Type IV, laser-perforated and partially demineralized bone. Results show that PPF wets easily, achieving 12.5% wt/wt in 30 min. Compressive tests on the PPF foam material showed that the compressive strength was 6.8 MPa prior to in vitro incubation but then gradually reduced to 1.9 MPa at 8 weeks. Push-out and pulloff strength tests showed that initially both PPF and PLGA foam coatings had comparable adherence strengths to the cortical bone samples (100-150 N). When additional geometrical surface alteration by perforation and demineralization of the bony substrate was employed, in vitro adherence of the PPF foam coating was further increased to 120 N, demonstrating a statistically significant improvement of push-out strength throughout the entire 8-week observation period ($p<0.0002$ for all four data points). The pore geometry of PPF-foam coatings changed little over the 2-month evaluation period. In comparison, PLGA foam coating around the cortical bone samples rapidly lost structure with a decrease of 67% in strength seen after 1-week in vitro incubation. These new types of bone allografts may be particularly useful where the use of other replacement materials is not feasible or practical.

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1: J Biomater Sci Polym Ed. 2000;11(4):401-14.

Tissue responses to molecularly reinforced polylactide-co-glycolide implants.

Lewandrowski KU, **Gresser JD**, **Wise DL**, **Trantolo DJ**, **Hasirci V**.

Orthopaedic Research Laboratories, Massachusetts General Hospital, Boston 02114, USA.

Plates for internal fixation fabricated from biodegradable polymers degrade via an autocatalytic route. When they are used in bone implants of significant size and thickness, hollowing of the implant may occur while the overall dimensions appear unchanged. We hypothesized that incorporation of a cross-linked polypropylene fumarate matrix into polylactide-co-glycolide bone plates may provide an internal molecular network which prevents implant collapse. Cross-linking reagents of varying hydrophilicity including N-vinylpyrrolidone (VP), hydroxyethylmethacrylate (HEMA), and ethyleneglycol dimethacrylate (EGDMA) were employed. With the objective of determining the most biocompatible and structurally sound composition for molecular reinforcement, we investigated tissue responses in both subcutaneous and orthotopic rodent implantation models in relation to maintenance of implant integrity by histologic, histomorphometric, and stereomicroscopic analysis. Results showed that tissue responses were correlated with dimensional stability of the implants. The most favorable results were seen with the hydrophobic cross-linker EGDMA; this may have been related to the initial reduction of the water uptake by the implant. Cross-linking of polypropylene fumarate with EGDMA within a polylactide-co-glycolide bone plate may offer a means to maintain excellent biocompatibility while improving dimensional stability of biodegradable bone plates.

PMID: 10903038 [PubMed - indexed for MEDLINE]

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1: Tissue Eng. 2001 Aug;7(4):385-94.

Expression of liver-specific functions by rat hepatocytes seeded in treated poly(lactic-co-glycolic) acid biodegradable foams.

Hasirci V, Berthiaume F, Bondre SP, Gresser JD, Trantolo DJ, Toner M, Wise DL.

Department of Biological Sciences, Biotechnology Research Center, Middle East Technical University, Ankara, Turkey.

Techniques of liver replacement would benefit patients awaiting donor livers and may be a substitute for transplantation in patients whose livers can regenerate. Poly(lactic-co-glycolic acid) (PLGA) copolymers are biodegradable and have been shown to be useful as scaffolds for seeding and culturing various types of cells. In this study, foam disks were prepared from PLGA (lactic-to-glycolic mole ratio of 85:15) by lyophilization of benzene (5% w/v) solutions. These disks were then used as scaffolds for rat hepatocyte culture. Foams were coated with either a type I collagen gel (0.1% w/v), coated with gelatin (5% w/v), or treated with oxygen plasma (25 W, 90 s) to modify their surface chemistry and wettability. The disks were then seeded with rat hepatocytes (10(6)/mL) and cultured for a period of 2 weeks. All surface treatments resulted in increased hydrophilicity, the greatest being obtained by collagen treatment (contact angle < 10 degrees), and a minimal decrease in void fraction (5%). DNA content after a 2-week culture period increased proportionally with the wettability of the treated foam surface. Urea synthesis in untreated foams averaged 15.3 +/- 2.3 microg/h/microg DNA, which was significantly higher than that for controls, whereas gelatin and collagen treated foams exhibited urea synthetic rates below the control levels at all times. The DNA content decreased significantly by about 50% between days 1 and 12. PLGA foams, treated and untreated, represent a promising scaffold for scaling up hepatocyte cultures.

Related Links

Growth and metabolism of human hepatocytes on biomodified collagen poly (lactic-co-glycolic acid) three-dimensional scaffolds [ASAIO J. 2006]

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